Amendments to Drawings

Please replace FIG. 8 with the attached drawing. The drawing was amended to remove the shading from the rectangular box and the arrowheads.

Attachment: Replacement sheet

Remarks

Claims 1-13, 22, and 23 were pending in this application. Claim 1 is amended herein. Claims 2 and 14-21 are canceled herein. Claim 1 has been amended to incorporate the limitations of claim 2. Claims 3-6, 7, 12 and 22 are amended to depend from claim 1.

Applicants believe no new matter is introduced by the foregoing amendments. After entry of this amendment, **claims 1, 3-13, 22 and 23 are pending in this application.** Reconsideration of the pending claims is requested.

Specification

The Office action objects to the specification as not specifying the accession numbers of the deposits on page 44. Plasmids PL 451 and PL452 were deposited in accordance with the Budapest Treaty with the American Type Culture Collection (ATCC) on February 6, 2003. The specification is amended herein to state that the deposits were made with the ATCC in accordance with the Budapest treaty, to provide the deposit date, and to provide the accession numbers. Applicants believe that the amendment of the specification renders the objection moot.

Drawings

Fig. 8 was objected to for including grayscale that makes the text difficult to read. Submitted herewith is a replacement Fig. 8, wherein the shading is removed. No additional changes have been made to the replacement Fig. 8.

Rejection under 35 U.S.C. § 102(a)

Claims 1, 3, 4, and 13 were rejected under 35 U.S.C. § 102(a) as allegedly being anticipated by Cassanova et al. Applicants respectfully disagree with this rejection.

In order to expedite prosecution, submitted herewith is a Declaration Under 37 C.F.F. § 1.131, documenting that the inventors conceived of, and reduced to practice, a method for generating a vector for conditional knockout of a gene in a cell including a de-repressible promoter operably linked to a nucleic acid encoding Beta and Exo prior to February 13, 2002, in

the United States. The Declaration is signed by Drs. Court, Lee, and Liu. Drs. Copeland and Jenkins have relocated to Singapore. Dr. Liu and the undersigned have contacted Drs. Copeland and Jenkins; a copy of the Declaration signed by Drs. Copeland and Jenkins will be submitted shortly. The Declaration was sent to Dr. Ellis at her last known residence address. Unfortunately, Dr. Ellis has moved from this address and a forwarding address was not available. The Applicants will continue to try to locate Dr. Ellis to obtain her signature.

Applicants respectfully request that the Declaration Under 35 U.S.C. § 1.131 be considered. Applicants respectfully request that Examiner Dunston contact the undersigned to discuss an appropriate course of action if Dr. Ellis cannot be located.

Applicants submit that the Declaration under 35 U.S.C. § 1.131 will remove Cassanova et al. as a reference, thereby rendering the rejection moot.

Rejections Under 35 U.S.C. § 103

Claims 1-10, 12, 13, 22 and 23 are rejected under 35 U.S.C. § 103(a) as allegedly being obvious over Cassanova et al., in view of Lee et al. as evidenced by Buchholz et al. Applicants respectfully disagree with this rejection.

As described above, submitted herewith is a Declaration Under 37 C.F.R. § 1.131 that removes Cassanova et al as a reference. Thus, Cassanova et al. is not available as prior art.

Lee et al. teach a de-repressible promoter (pL) operably linked to a nucleic acid encoding Beta, Exo and Gam under the control of a temperature sensitive repressor. Lee et al. teach that this method can be used to introduce the arabinose promoter operably linked to Cre, and describe the introduction of a FRT-Kan-FRT cassette into a gene in a bacterial artificial chromosome. However, Lee et al. do not suggest, or render obvious inserting a nucleic acid encoding a selectable marker flanked by a pair of second recombining sites and a first recombining site into a second site in the gene. In addition, Lee et al. do not suggest, nor render obvious, excising the nucleic acid encoding the selectable marker with a second recombinase specific for the second recombining sites, wherein two first recombining sites remain in the gene following excision of the nucleic acid encoding the selectable marker, and wherein recombination of the two first recombining sites produces a nucleic acid sequence that cannot be transcribed to produce a functional protein

Buchholz et al. describes bacterial strains that produce FLP or Cre. Buchholz et al. does not describe methods for producing conditional knockouts of a gene, let alone disclose the use of a first and second pair of recombining sites to generate a conditional knockout. Thus, Buchholtz et al. does not make up the deficiencies of Lee et al.

Thus, Applicants submit that claims 1-10, 12, 13, 22 and 23 are not obvious over Lee et al., alone or in combination with Buchholz et al. Reconsideration and withdrawal of the rejection is respectfully requested.

Claims 1-4, 6-8, 10-13, 22 and 23 were rejected under 35 U.S.C. § 103(a) as allegedly being obvious over Cassanova et al. in view of Stewart et al. as evidenced by Buchholz et al.

As described above, a Declaration Under 37 C.F.R. § 1.131 is submitted herewith that removes Cassanova et al as a reference. Thus, Cassanova et al. is not available as prior art.

Stewart et al. teach a method of performing homologous recombination that utilizes an inducible promoter operably linked to Rec E/T. Stewart et al. teach that homologous recombination can be performed using BACs. However, Stewart et al. do not teach methods for generating vectors for conditional knock-outs, let alone methods that include (1) using homologous recombination to insert a nucleic acid encoding a selectable marker flanked by a pair of first recombining sites into a first site in a gene in a bacterial artificial chromosome, wherein a vector comprises the bacterial artificial chromosome, or (2) excising the nucleic acid encoding the selectable maker with a first recombinase specific for the first recombining sites, wherein a single first recombining site remains in the gene, or using homologous recombination to insert a nucleic acid encoding a selectable marker flanked by a pair of second recombining sites and a first recombining site into a second site in the gene, or (3) excising the nucleic acid encoding the selectable marker with a second recombinase specific for the second recombining sites such that two first recombining sites remain in the gene following excision of the nucleic acid encoding the selectable marker, wherein recombination of the two first recombining sites produces a nucleic acid sequence that cannot be transcribed to produce a functional protein.

Buchholz et al. describe bacterial strains that produce FLP or Cre. Buchholz et al. do not describe methods for producing conditional knockouts of a gene, let alone disclose the use of a first and second pair of recombining sites to generate a conditional knockout. Thus Buchholz et al. do not make up for the deficiencies of Stewart et al.

Thus, Applicants submit the 1-4, 6-8, 10-13, 22 and 23 are not obvious over Stewart et al., alone or in combination with Buchholz et al. Reconsideration and withdrawal of the rejection is respectfully requested.

Request for an Examiner Interview

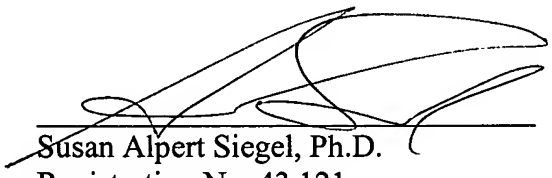
Applicants respectfully request that Examiner Dunston contact the undersigned to arrange an interview to discuss the outstanding rejections and the Declaration under 35 U.S.C. § 1.131. It is believed that a brief discussion of the merits of the present application will expedite prosecution and allowance of the claims.

Conclusion

It is respectfully submitted that the present claims are in a condition for allowance. In addition, the Examiner is formally requested to contact the undersigned prior to issuance of the next Office action in order to arrange a telephone interview. .

Respectfully submitted,

KLARQUIST SPARKMAN, LLP

By 

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